

Applicants : Michael Wayne Graham and Robert Norman Rice
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Filed : August 22, 2003
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Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-47. (Canceled)

48. (Currently Amended) A double-stranded synthetic DNA gene, comprising multiple copies of a structural gene region,
wherein the structural gene region comprises a nucleotide sequence which consists of greater than 20 consecutive nucleotides and which is identical to a nucleotide sequence of a target gene in a vertebrate animal cell,
wherein one of the copies is placed in the sense orientation and another of the copies is placed in the antisense orientation operably under the control of a single promoter sequence which is operable in the cell,
and wherein the copy of the structural gene region placed in the sense orientation and the copy of the structural gene region placed in the antisense orientation are arranged so as to form an interrupted palindrome sequence which is operably under the control of the single promoter sequence.

49-109. (Canceled)

110. (Currently Amended) A double-stranded ~~synthetic-genetic~~ DNA construct, comprising a synthetic DNA gene and a genetic sequence which provides for the maintenance and/or replication of the double-stranded synthetic genetic construct in prokaryotes or eukaryotes and/or the

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integration of the double-stranded DNA ~~synthetic genetic~~ construct or a part thereof into the genome of a eukaryotic cell or organism,

wherein the synthetic DNA gene comprises multiple copies of a structural gene region,

wherein the structural gene region comprises a nucleotide sequence which consists of greater than 20 consecutive nucleotides and which is identical to a nucleotide sequence of a target gene in a vertebrate animal cell,

wherein one of the copies is placed in the sense orientation and another of the copies is placed in the antisense orientation operably under the control of a single promoter sequence which is operable in the cell,

and wherein the copy of the structural gene region placed in the sense orientation and the copy of the structural gene region placed in the antisense orientation are arranged so as to form an interrupted palindrome sequence which is operably under the control of the single promoter sequence.

111-113. (Canceled)

114. (Currently Amended) The double-stranded DNA ~~synthetic genetic~~ construct of claim 110, wherein the genetic sequence comprises one or more origins of replication and/or selectable marker gene sequences.

115. (Currently Amended) The double-stranded DNA ~~synthetic genetic~~ construct of claim 110, which is encapsulated in a liposome.

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116. (Currently Amended) The double-stranded DNA ~~synthetic~~ ~~genetic~~ construct of claim 110, which is in a virus particle.
117. (Currently Amended) The double-stranded DNA ~~synthetic~~ ~~genetic~~ construct of claim 116, wherein the virus particle is an attenuated virus or associated with a virus coat.
118. (Currently Amended) The double-stranded DNA ~~synthetic~~ ~~genetic~~ construct of claim 110, which is in a recombinant viral vector.
119. (Currently Amended) The double-stranded DNA ~~synthetic~~ ~~genetic~~ construct of claim 118, wherein the recombinant viral vector is a retrovirus or a lentivirus.
120. (Currently Amended) The double-stranded DNA synthetic gene of claim 48, wherein the target gene is from a viral pathogen of the vertebrate animal cell.
121. (Currently Amended) The double-stranded DNA ~~synthetic~~ ~~genetic~~ construct of claim 110, wherein the target gene is from a viral pathogen of the vertebrate animal cell.
122. (Currently Amended) The double-stranded synthetic DNA gene of claim 48, wherein the promoter is selected from the group consisting of an SV40 late promoter, an SV40 early promoter, an RSV-LTR promoter and a CMV IE promoter.

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123. (Currently Amended) The double-stranded DNA ~~synthetic~~ ~~genetic~~ construct of claim 110, wherein the promoter is selected from the group consisting of an SV40 late promoter, an SV40 early promoter, an RSV-LTR promoter and a CMV IE promoter.
124. (Currently Amended) The double-stranded synthetic DNA gene according to claim 48, wherein the nucleotide sequence of the target gene encodes an amino acid sequence.
125. (Currently Amended) The double-stranded DNA ~~synthetic~~ ~~genetic~~ construct of claim 110, wherein the nucleotide sequence of the target gene encodes an amino acid sequence.
126. (Currently Amended) The double-stranded DNA synthetic gene of claim 48, wherein the nucleotide sequence of the target gene does not encode an amino acid sequence.
127. (Currently Amended) The double-stranded DNA ~~synthetic~~ ~~genetic~~ construct of claim 110, wherein the nucleotide sequence of the target gene does not encode an amino acid sequence.
128. (Currently Amended) The double-stranded synthetic DNA gene of claim 48, wherein the target gene is derived from the genome of a pathogen of the vertebrate animal cell.
129. (Currently Amended) The double-stranded DNA ~~synthetic~~ ~~genetic~~ construct of claim 110, wherein the target gene is derived from the genome of a pathogen of the human-vertebrate animal cell.

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130. (Currently Amended) The double-stranded synthetic DNA gene of claim 48, wherein the target gene is endogenous to the genome of the vertebrate animal cell.

131. (Currently Amended) The double-stranded DNA ~~synthetic genetic~~ construct of claim 110, wherein the target gene is endogenous to the genome of the vertebrate animal cell.

132. (Currently Amended) A composition comprising the double-stranded DNA ~~synthetic genetic~~ construct of claim 110 and a carrier, excipient or diluent suitable for human application.

133. (Currently Amended) A vertebrate animal cell in cell or tissue culture, comprising a double-stranded synthetic DNA gene which comprises multiple copies of a structural gene region,

wherein the structural gene region comprises a nucleotide sequence which consists of greater than 20 consecutive nucleotides and which is identical to a nucleotide sequence of a target gene in the cell,

wherein one of the copies is placed in the sense orientation and another of the copies is placed in the antisense orientation operably under the control of a single promoter sequence which is operable in the cell,

and wherein the copy of the structural gene region placed in the sense orientation and the copy of the structural gene region placed in the antisense orientation are arranged in the structural region so as to form an interrupted palindrome sequence which is operably under the control of the single promoter sequence.

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134. (Previously Presented) The vertebrate animal cell of claim 133, wherein the structural gene region is transcribed in the cell.
135. (Previously Presented) The vertebrate animal cell of claim 133, wherein the cell has a reduced level of expression of the target gene.
136. (Previously Presented) The vertebrate animal cell of claim 133, wherein the structural gene region placed in the sense orientation and the structural gene region placed in the antisense orientation are separated by a sequence of nucleotides.
137. (Canceled)
138. (Previously Presented) The vertebrate animal cell of claim 136, wherein the sequence of nucleotides separating the structural gene region placed in the sense orientation and the structural gene region placed in the antisense orientation is 10-50 nucleotides in length, 50-100 nucleotides in length, or 100-500 nucleotides in length.
139. (Withdrawn; Currently Amended) A process of modifying a vertebrate animal cell in cell or tissue culture, comprising the step of introducing the double-stranded synthetic DNA gene of claim 48 into the cell.
140. (Withdrawn; Currently Amended) A process of modifying a vertebrate animal cell in cell or tissue culture comprising the step of introducing the double-stranded DNA ~~genetic~~ construct of claim 110 into the cell.

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141-144. (Canceled)

145. (Withdrawn; Previously Presented) A process of modifying a vertebrate animal cell, comprising contacting the cell with the composition of claim 132.

146. (Currently Amended) The double-stranded synthetic DNA gene of claim 48, wherein the cell is a human cell.

147. (Currently Amended) The double-stranded DNA ~~synthetic genetic~~ construct of claim 110, wherein the cell is a human cell.

148. (Previously Presented) The cell of claim 133, which is a human cell.

149. (Previously Presented) The cell of claim 133, which is an embryonic stem cell, cultured skin fibroblast, neuronal cell, somatic cell, hematopoietic stem cell or T-cell.

150. (Withdrawn; Currently Amended) A process for selecting an appropriate nucleotide sequence for repressing, delaying or otherwise reducing expression of a target gene in a cell, comprising the steps of obtaining the double-stranded synthetic DNA gene of claim 48, introducing the double-stranded synthetic DNA gene into the cell, and assaying the cell for efficacy of the double-stranded synthetic DNA gene in repressing, delaying or otherwise reducing target gene expression, thereby selecting an appropriate nucleotide sequence for repressing, delaying or otherwise reducing expression of a target gene in the cell.

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151. (Withdrawn; Currently Amended) The process of claim 150, wherein the double-stranded synthetic DNA gene is comprised in a set of diverse double-stranded synthetic DNA genes each according to claim 48, wherein each member of the set is contained within a plasmid, cosmid, bacteriophage or virus vector molecule which is suitable for maintenance and/or replication in a cellular host.
152. (Withdrawn; Currently Amended) A process for identifying the function of a target gene in specifying a phenotype in a cell, comprising the steps of obtaining the double-stranded synthetic DNA gene of claim 48, introducing the double-stranded synthetic DNA gene into the cell, and assaying the cell for a phenotype, thereby identifying the function of a target gene in specifying a phenotype in the cell.